

AMENDMENTS TO THE CLAIMS

Claim 1 (Currently Amended) A suspension comprising fibrinogen, thrombin and alcohol, the suspension having been obtained by a method comprising:

- providing a fibrinogen mixture of fibrinogen and an alcohol,
- providing a thrombin mixture of thrombin and an alcohol,
- mixing the fibrinogen mixture and the thrombin mixture; so as to obtain the said suspension, the suspension containing fibrinogen and thrombin particles, the Folk Ward mean diameter of the particles being 25 - 100 μm .

Claim 2 (Original) A suspension according to claim 1, wherein the Folk Ward mean diameter of the particles is 35 - 80 μm .

Claim 3 (Original) A suspension according to claim 1, wherein the viscosity of the suspension is so that a volume of 90 - 120 ml of suspension, when influenced by gravity only, exits through a bottom opening of a container having

- a cylindrical portion with an inner diameter of 40 - 50 mm and a height of 55 - 65 mm, and
- a conical bottom portion with a height of 17 - 23 mm, whereby the bottom opening is provided at the lower end of the conical portion as a circular opening with a diameter of 2 - 3 mm,

in 25 - 75 seconds.

Claim 4 (Original) A suspension according to claim 3, wherein said volume of suspension exits through the bottom opening in 30 - 50 seconds.

Claim 5 (Original) A suspension according to claim 1, further comprising aprotinin.

Claim 6 (Original) A method of preparing a suspension with fibrinogen and thrombin, comprising:

- providing a fibrinogen mixture of fibrinogen and an alcohol,

- providing a thrombin mixture of thrombin and an alcohol,
- mixing the fibrinogen mixture and the thrombin mixture, so as to obtain said suspension, so as to obtain a suspension containing fibrinogen and thrombin particles, the Folk Ward mean diameter of the particles being 25 - 100 μm .

Claim 7 (Original) A method according to claim 6, wherein, at the step of providing the fibrinogen mixture, the fibrinogen is pre-micronised so as to obtain particles having a Folk Ward mean diameter of 25-100 μm .

Claim 8 (Original) A method according to claim 6, wherein the pre-micronised fibrinogen is stirred into the alcohol to obtain said fibrinogen mixture.

Claim 9 (Original) A method according to claim 6, wherein, at the step of providing the mixture, the mixture is homogenized.

Claim 10 (Original) A method according to claim 9, wherein the mixture is homogenized at a temperature between 0°C and 12°C.

Claim 11 (Original) A method according to claim 10, wherein the mixture is homogenized at a temperature between 2°C and 8°C.

Claim 12 (Original) A method according to claim 11, wherein the temperature is lowered during homogenization.

Claim 13 (Original) A method according to claim 6, wherein the thrombin comprises at least one of: human thrombin, bovine thrombin, and recombinant thrombin.

Claim 14 (Original) A method according to claim 6, wherein the fibrinogen comprises at least one of: human fibrinogen and recombinant fibrinogen.

Claim 15 (Original) A method according to claim 6, wherein the suspension further comprises aprotinin.

Claim 16 (Original) A method according to claim 6, wherein the alcohol is an ethanol.

Claim 17 (Original) A method according to claim 16, wherein the ethanol is an anhydrous ethanol.

Claim 18 (Original) A method according to claim 6, wherein the step of mixing fibrinogen mixture and the thrombin mixture is carried out while stirring the suspension.

Claim 19 (Original) A method according to claim 18, wherein the stirring is carried out at a temperature between 0°C and 12°C.

Claim 20 (Original) A method according to claim 19, wherein the stirring is carried out at a temperature between 2° and 8°C.

Claim 21 (Currently Amended) A method for coating a carrier with a suspension comprising fibrinogen and thrombin, wherein the suspension has been derived from a method comprising the steps of:

- providing a fibrinogen mixture of fibrinogen and an alcohol,
- providing a thrombin mixture of thrombin and an alcohol,
- mixing the fibrinogen mixture and the thrombin mixture; so as to obtain the said suspension, wherein the so as to obtain a suspension contains containing fibrinogen and thrombin particles, the Folk Ward mean means diameter of the particles being 25 - 100 μm ,
the method of coating comprising:

- providing the suspension of fibrinogen, thrombin and an alcohol at a location near the carrier,
and
- applying the said suspension to a coating surface of the carrier.

Claim 22 (Original) A method according to claim 21, wherein the carrier is a collagen carrier.

Claim 23 (Original) A method according to claim 22, wherein the collagen carrier is a collagen sponge.

Claim 24 (Currently Amended) A method according to claim 23, wherein the collagen sponge fulfils at least one of the following criteria:

- pH-value between 5.0 and 6.0,
- lactic acid content at the most 5%,
- ammonium content at the most 0.5%,
- soluble protein content, calculated as albumin content, at the most 0.5%,
- sulphate ashes content at the most 1.0%,
- heavy metal content at the most 20 ppm,
- microbiological purity; at the most 10^3 CFU/g,
- collagen content of 75 to 100%,
- density of 1 to 10 mg/cm³, and
- elasticity modulus module in the range of 5-100 N/cm.

Claim 25 (Currently Amended) A method according to claim 23, wherein the carrier is a collagen sponge, and wherein the collagen sponge has been derived from a method comprising the steps of:

preparing a collagen gel,

- mixing air into the collagen gel; so as to obtain a collagen foam,
- drying the collagen foam; so as to obtain a dry block of carrier having chambers therein, and

- isolating, from the block of collagen sponge, parts of sponge showing at least one of:
 - a chamber diameter of more than 0.75 mm and less than 4 mm, and
 - chambers of an average diagonal dimension of 3 mm.

Claim 26 (Original) A method according to claim 21, wherein the step of applying the suspension to the carrier is performed at an ambient temperature of 0° - 12°C.

Claim 27 (Original) A method according to claim 26, wherein the step of applying the suspension to the carrier is carried out at an ambient temperature of 1° - 10°C.

Claim 28 (Original) A method according to claim 27, wherein the step of applying the suspension to the carrier is carried out at an ambient temperature of 2° - 8°C.

Claim 29 (Original) A method according to claim 21, wherein the step of applying the suspension to the carrier is carried out in an ambient atmosphere with a relative humidity of 75 - 99%.

Claim 30 (Original) A method according to claim 29, wherein the step of applying the suspension to the carrier is carried out in an ambient atmosphere with a relative humidity of 85 - 95%.

Claim 31 (Currently Amended) A method according to claim 21, wherein a volume of 0.08 ml - 0.12 ml of suspension is applied to the carrier per pr. cm² of the coating surface.

Claim 32 (Currently Amended) A method according to claim 21, wherein the suspension is distributed evenly over a given width of the coating surface; so that the mass of fibrinogen per area unit of the coating surface varies at most 25%.

Claim 33 (Currently Amended) A method according to claim 21, wherein an applicator comprising at least one jet is used for applying the suspension to the carrier, and wherein whereby the suspension is forced through the jet while the carrier and the jet are moved relative to each other.

Claim 34 (Original) A method according to claim 21, wherein an applicator comprising a container having a plurality of separate outlets is used for applying the suspension to the carrier, and wherein the suspension is forced from the container through the outlets onto the carrier.

Claim 35 (Original) A method according to claim 34, wherein the carrier and the applicator are moved relative to each other in a transport direction while the suspension is being applied to the carrier.

Claim 36 (Original) A method according to claim 35, wherein the rate of movement is 0.025 m/s - 0.05 m/s.

Claim 37 (Original) A method according to claim 36, wherein the rate of movement is 0.03 - 0.04 m/s.

Claim 38 (Original) A method according to claim 34, wherein the flow rate of suspension applied to the carrier through the applicator is 400 - 600 ml/min.

Claim 39 (Original) A method according to claim 38, wherein the flow rate is 470 - 550 ml/min.

Claim 40 (Original) A method according to claim 39, wherein the flow rate is 495 - 505 ml/min.

Claim 41 (Currently Amended) A method of drying a suspension of fibrinogen, thrombin and an alcohol applied as a wet coating on a coating surface of a carrier, the suspension containing

fibrinogen and thrombin particles, the Folk Ward mean diameter of the particles being 25-100 μ m, the method comprising the step of:

submitting the coated carrier to a pressure below 1000 mbar, so as to obtain a dried coating surface on the carrier, so as to fixate the dried coating to the coating surface.

Claim 42 (Currently Amended) A method according to claim 41, wherein the suspension has been obtained by:

- providing a fibrinogen mixture of fibrinogen and an alcohol,
- providing a thrombin mixture of thrombin and an alcohol,
- mixing the fibrinogen mixture and the thrombin mixture; so as to obtain the said suspension, and

and wherein the carrier is a collagen sponge which has been derived from a method comprising the steps of:

- preparing a collagen gel,
- mixing air into the collagen gel; so as to obtain a collagen foam,
- drying the collagen foam; so as to obtain a dry block of collagen sponge having chambers therein,
- isolating, from the block of collagen sponge, parts of sponge showing at least one of:
 - a chamber diameter of more than 0.75 mm and less than 4 mm, and
 - a chamber with an average diagonal dimension of 3 mm,

and wherein the coating has been applied to the collagen sponge by:

- providing the suspension of fibrinogen, thrombin and an alcohol at a location near the collagen sponge, and
- applying the suspension to the coating surface of the collagen sponge.

Claim 43 (Original) A method according to claim 41, wherein the coated carrier is submitted to said pressure at a temperature of 0°C - 12°C.

Claim 44 (Original) A method according to claim 43, wherein the coated carrier is submitted to said pressure at a temperature of 1°C - 10°C.

Claim 45 (Original) A method according to claim 44, wherein the coated carrier is submitted to said pressure at a temperature of 2° - 8°C.

Claim 46 (Original) A method according to claim 41, wherein the coated carrier is submitted to said pressure at a relative humidity of the surrounding atmosphere of 75 - 99%.

Claim 47 (Original) A method according to claim 41, wherein the coated carrier is submitted to said pressure at a relative humidity of the surrounding atmosphere of 85 - 95%.

Claim 48 (Currently Amended) A method according to claim 41, wherein a flow of air passes across the coated carrier during drying.

Claim 49 (Original) A method according to claim 43, wherein the coated carrier is kept at said temperature for a period of at least 1 hour.

Claim 50 (Original) A method according to claim 43, wherein the coated carrier is kept at said temperature for a period of at least 2 hours.

Claim 51 (Original) A method according to claim 43, wherein the coated carrier is kept at said temperature for a period of at least 4 hours.

Claim 52 (Original) A method according to claim 41, wherein the area of the dried coating surface is at least 75% the size of the area of the wet coating surface.

Claim 53 (Original) A method according to claim 41, wherein the area of the dried coating surface is at least 80% the size of the area of the wet coating surface.

Claim 54 (Original) A method according to claim 41, wherein the carrier and the dried coating surface have a water content not exceeding 12% by weight.

Claim 55 (Original) A method according to claim 41, wherein the carrier and the dried coating surface have a water content not exceeding 8% by weight.

Claim 56 (Original) A method according to claim 41, wherein the suspension further comprises aprotinin.

Claim 57 (Original) A coated collagen sponge with a coating of fibrinogen and thrombin, wherein the coated collagen sponge has been obtained by a method comprising the steps of:

- providing a collagen sponge by a method comprising:
 - preparing a collagen gel,
 - mixing air into the collagen gel, so as to obtain a collagen foam,
 - drying the collagen foam, so as to obtain a dry block of collagen sponge having chambers therein,
 - isolating, from the block of collagen sponge, parts of sponge showing at least one of:
 - a chamber diameter of more than 0.75 mm and less than 4 mm, and
 - a chamber with an average diagonal dimension of 3 mm,
- applying a suspension of fibrinogen, thrombin and an alcohol to a coating surface of the collagen sponge, and
- submitting the coated carrier to a pressure below 1000 mbar, so as to obtain a dried coating surface on the carrier, so as to fixate the dried coating to the coating surface,
the coated collagen sponge having at least one of the following properties:

- the suspension is distributed evenly over a given width of the coating surface, so that the mass of fibrinogen per area unit of the coating surface varies at most 25%,
- the abrasion of the coating is less than 2.0 mg/cm² when a sample of 1x5cm² of the coated material is shaken in a test-tube on a Vibrofix shaker at a frequency of 800 - 1200 rpm for 2 minutes.

Claim 58 (Original) A coated collagen sponge according to claim 57, wherein the suspension has a water content of 20 - 80 mg/ml.

Claim 59 (Original) A coated collagen sponge according to claim 57, wherein the suspension has a water content of 24 - 32 mg/ml.

Claim 60 (Original) A coated collagen sponge according to claim 57, wherein the thrombin content of the suspension is 20 - 40 I.U./ml.

Claim 61 (Original) A coated collagen sponge according to claim 57, wherein said thrombin content is 24 - 33 I.U./ml.

Claim 62 (Original) A coated collagen sponge according to claim 57, wherein the thrombin content is 2 - 4 I.U./cm² in average over the coating surface.

Claim 63 (Original) A coated collagen sponge according to claim 57, wherein the thrombin content is 2.3 - 3.3 I.U./cm² in average over the coating surface.

Claim 64 (Original) A coated collagen sponge according to claim 57, wherein the thrombin content does not exceed 5 I.U./cm² at any location on the coating surface.

Claim 65 (Original) A coated collagen sponge according to claim 57, wherein the thrombin content does not exceed 3.8 I.U./cm² at any location on the coating surface.

Claim 66 (Original) A coated collagen sponge according to claim 57, wherein the microbiological purity of the coated carrier is 4 CFU/cm², at the most.

Claim 67 (Original) A coated collagen sponge according to claim 57, wherein the microbiological purity of the coated carrier is 2.25 CFU/cm², at the most.